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Validation of a fresh-frozen tissue based prognostic gene signature in formalin-fixed, paraffin-embedded melanomas

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Abstract

Histopathological staging of melanoma is limited in predicting outcome, and complementary molecular markers are not available for routine prognostic assessment. We have recently identified and validated a prognostic nine-gene signature expressed in fresh-frozen primary cutaneous melanomas (training cohort: n=91; validation cohort: n=44). A signature-based risk score predicts patient overall survival independently of AJCC staging (multivariate regression analysis: p = 0.0004; hazard ratio: 3.8). The purpose of the present study was to establish signature expression analysis in formalin-fixed, paraffin-embedded (FFPE) melanomas to validate prognostic significance of the signature-based risk score.

From FFPE melanomas matching the training and validation cohorts of the above study (n=125), RNA was prepared and transcribed into cDNA. Following cDNA pre-amplification, expression of the 9 signature genes, 2 additional candidate genes, and 3 housekeeping genes was quantified by real-time PCR. Correlation of gene expression with overall survival was evaluated using Cox regression analysis.

Expression of a signature of 8 out of 11 genes was significantly associated with overall survival in univariate Cox regression analysis. A signature based risk-score predicted overall survival independently of AJCC staging (multivariate analysis: p=0.007, hazard ratio 3.0). Thus, the fresh-frozen tissue based prognostic gene signature was successfully validated in FFPE melanomas.

We have established a quantitative, robust prognostic score, based on FFPE melanomas, that is complementary to AJCC in predicting outcome. This greatly increases clinical applicability and allows retrospective prognostic assessment of melanomas. The score identifies patients at low risk, not identified by AJCC staging, and defines high-risk patients in need of adjuvant therapy.

Biography

Georg Brunner has completed his PhD in Germany and postdoctoral studies at the German Cancer Research Center in Heidelberg. He spent more than 8 years abroad, as Research Assistant Professor at NYU and Lecturer at Manchester University in the UK. He is the Head of Research at the Skin Cancer Center Hornheide-Münster in Germany. He has published more than 50 papers in reputed journals and is inventor on 3 International Patents.